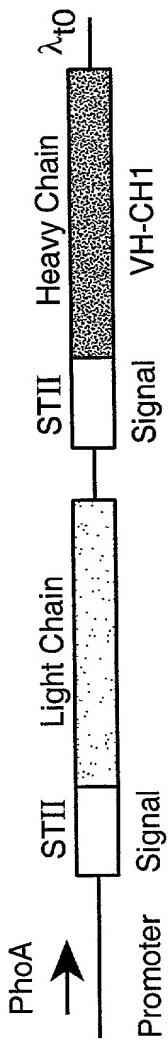


Fab Expression Vector pAK19



Full Length Antibody Expression Vector Derived from pAK19

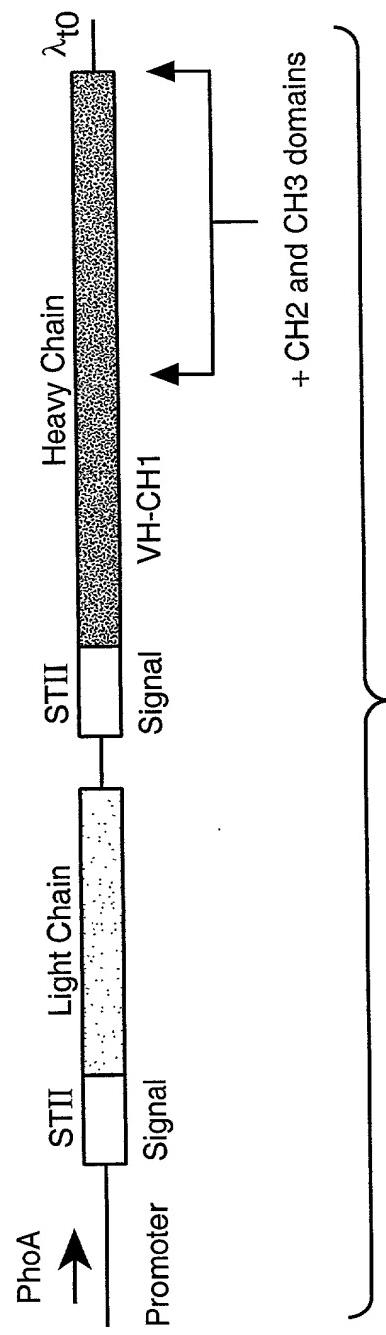
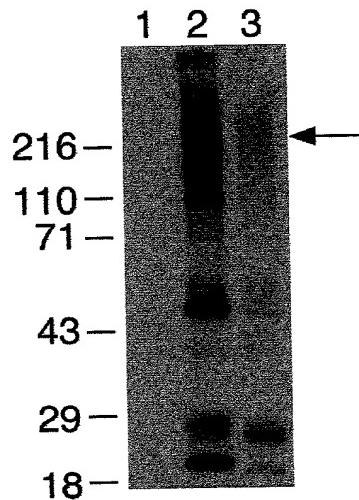
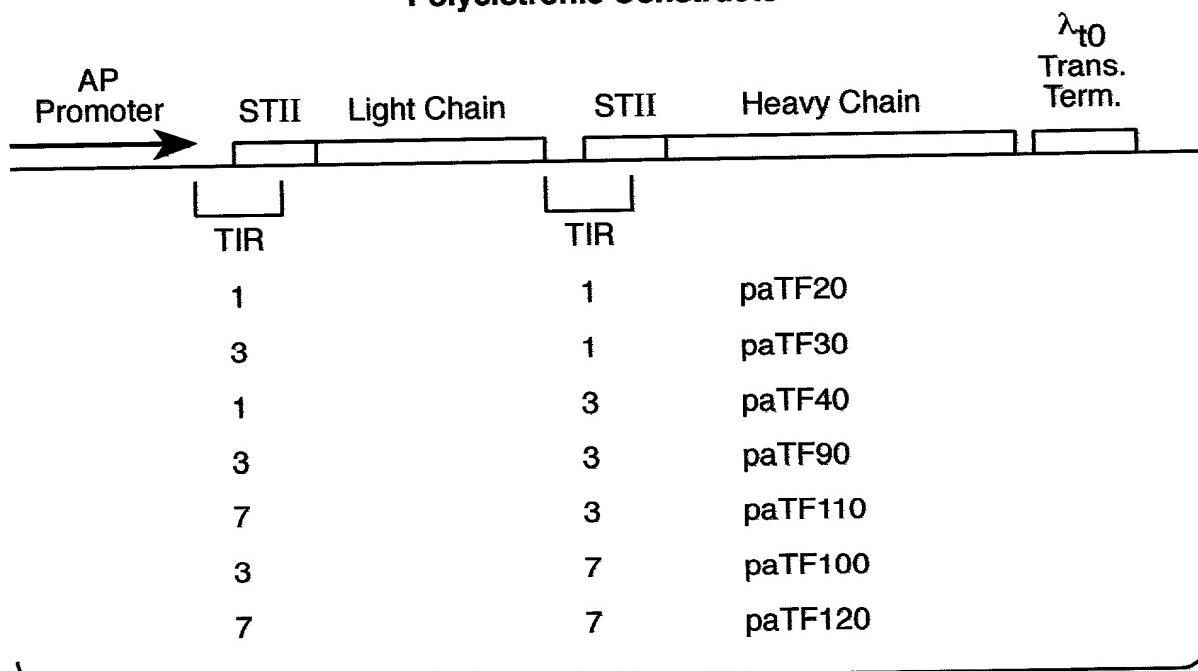


FIG. - 1

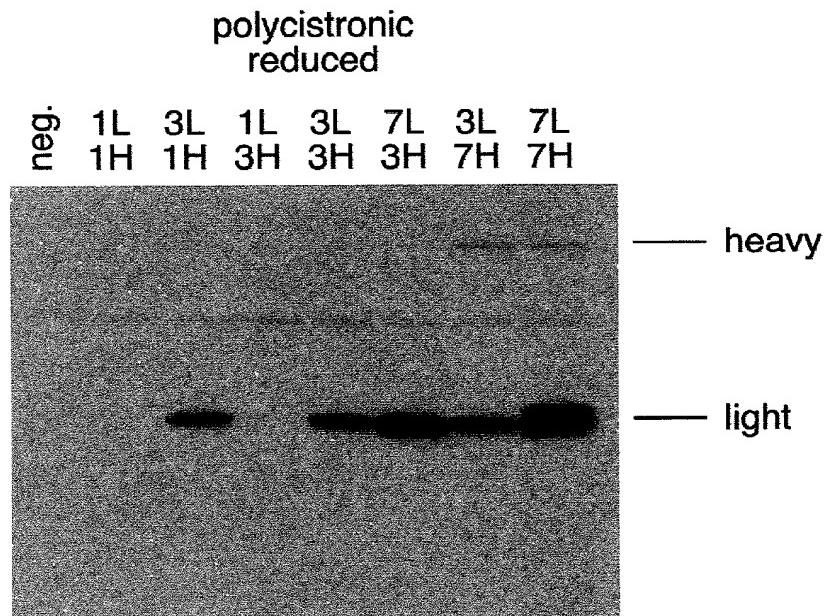
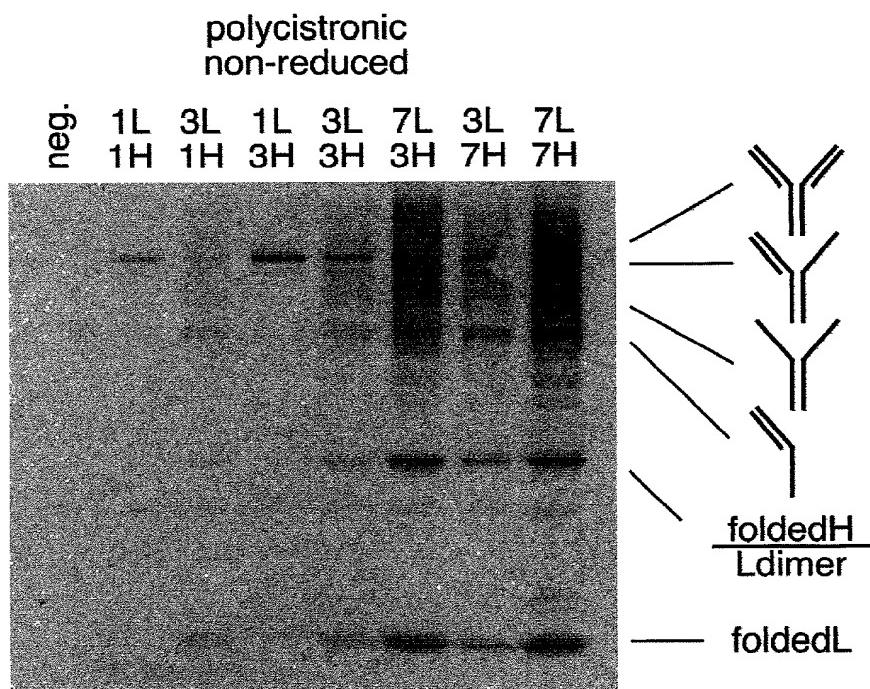
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**FIG._2****Polycistronic Constructs****FIG._3**

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FIG._4A**FIG._4B**

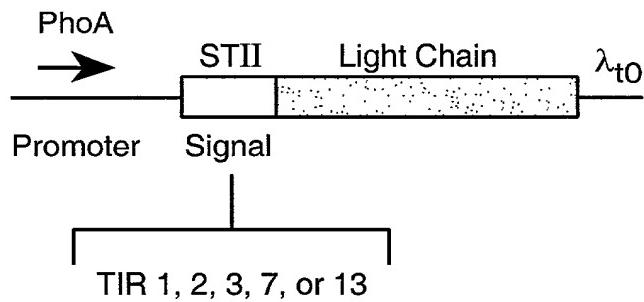
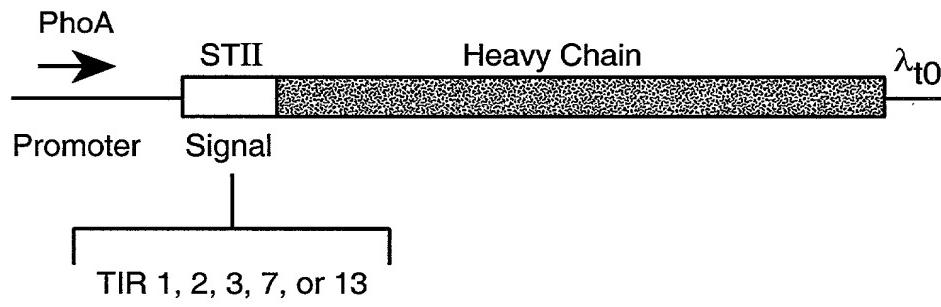
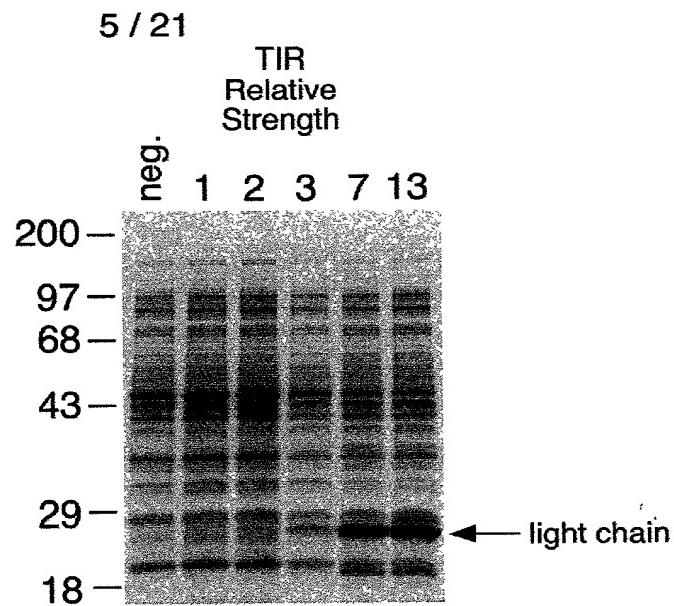
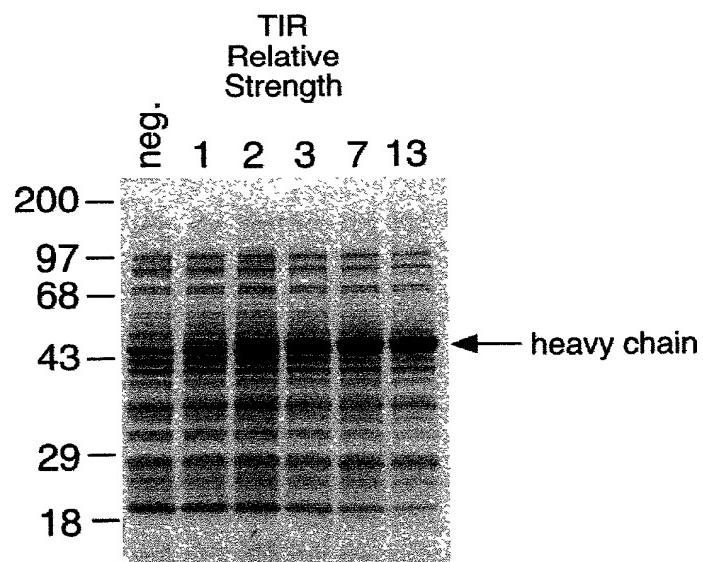
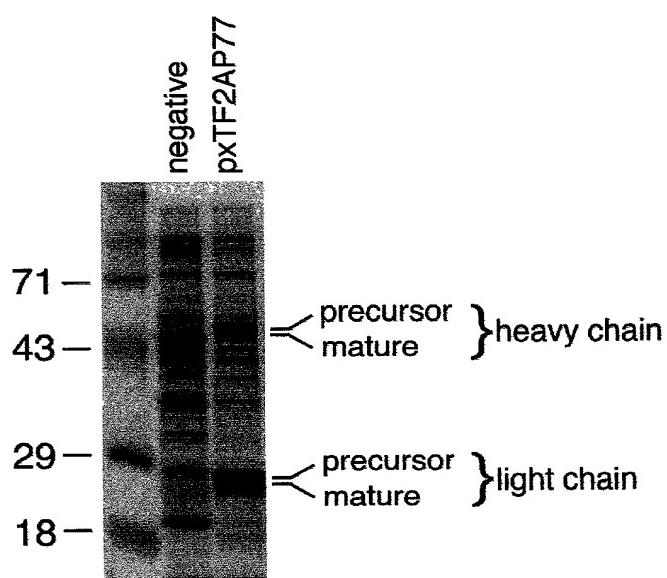
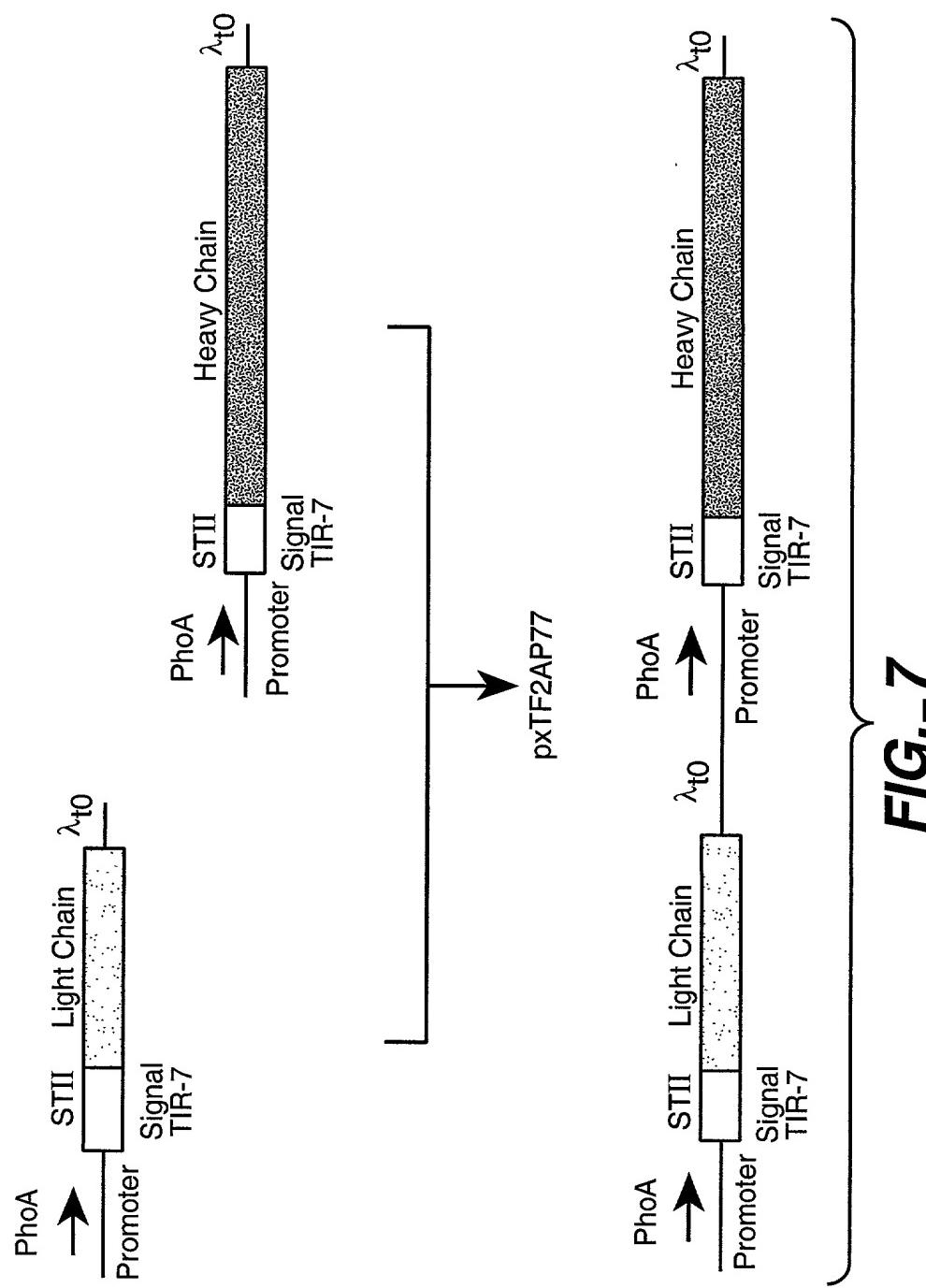
Light Chain Constructions**Heavy Chain Constructions**

FIG._5

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FIG._6A**FIG._6B****FIG._8**

**FIG.-7**

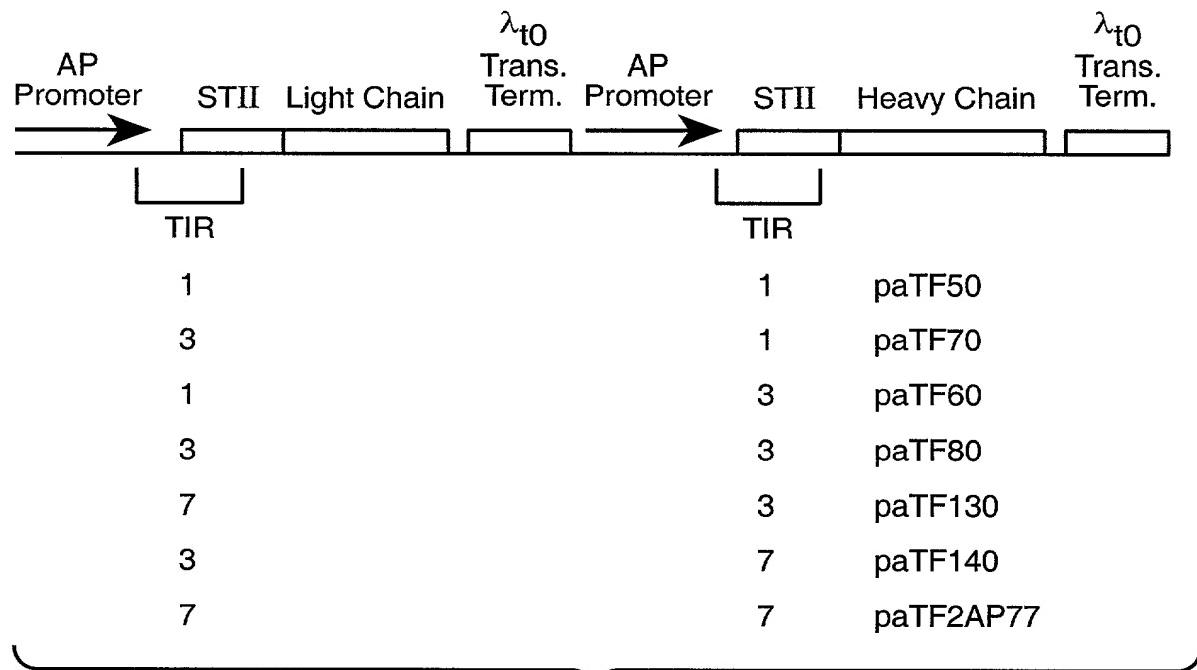
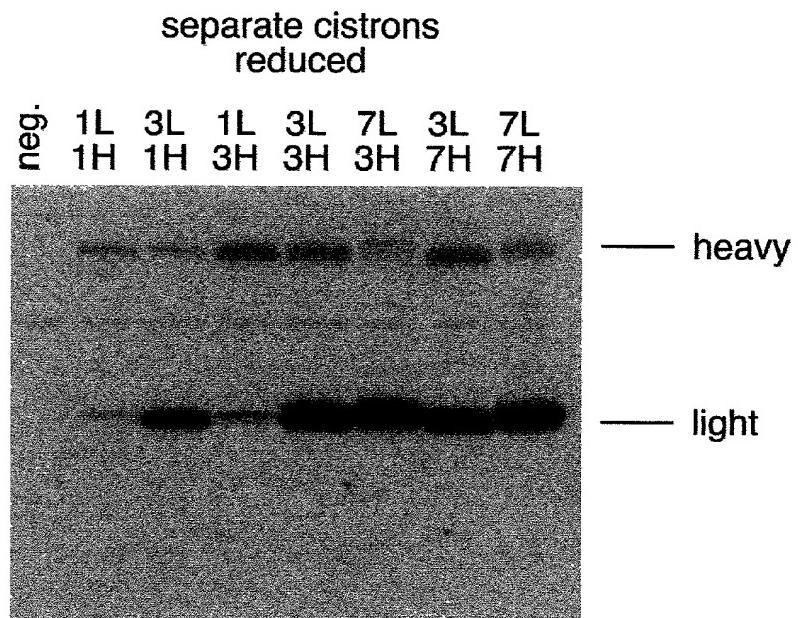
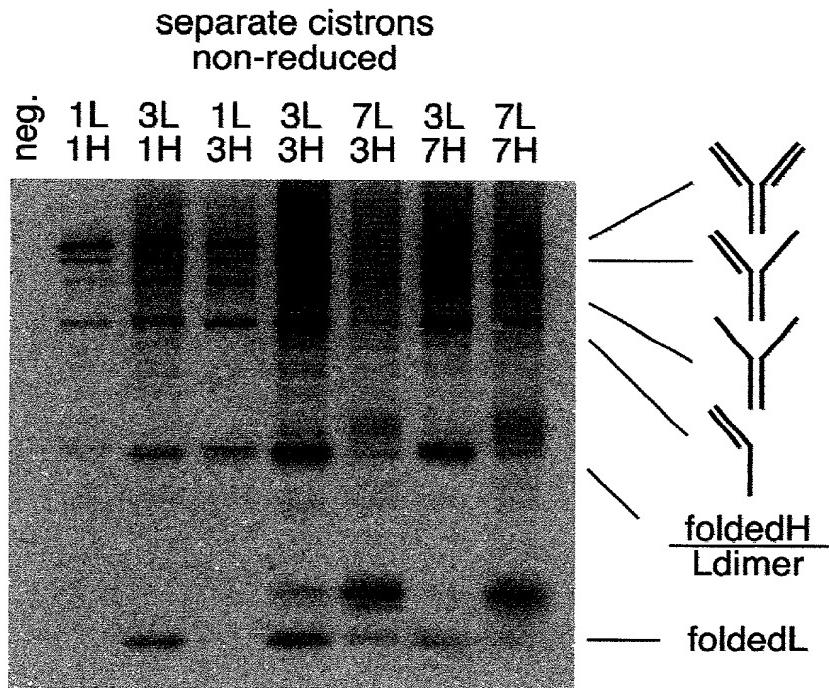
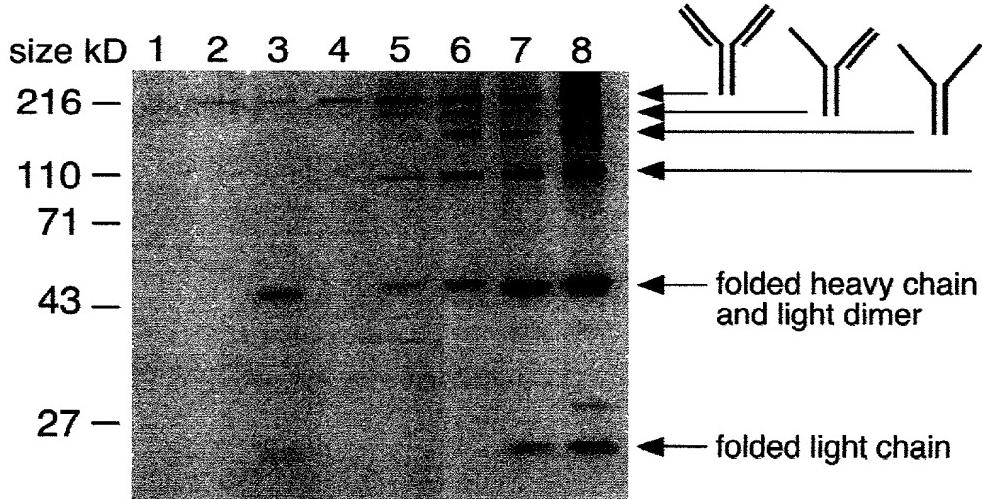
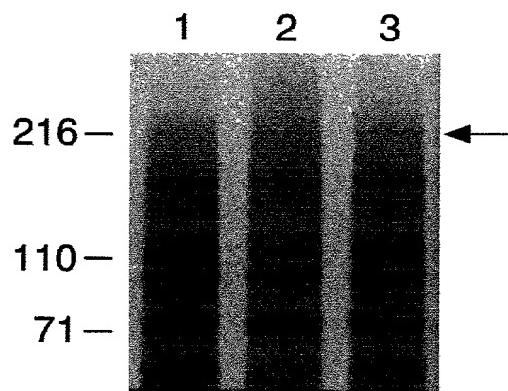
Separate Cistron Constructs**FIG._9**

FIG._10A**FIG._10B**

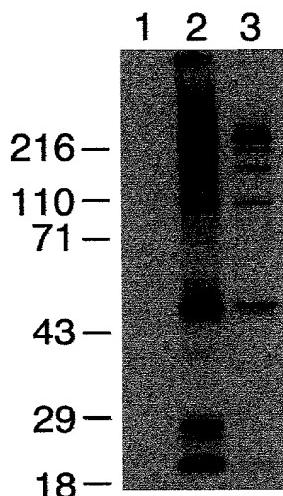
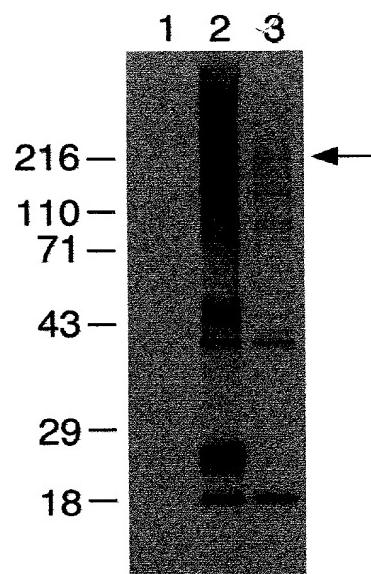
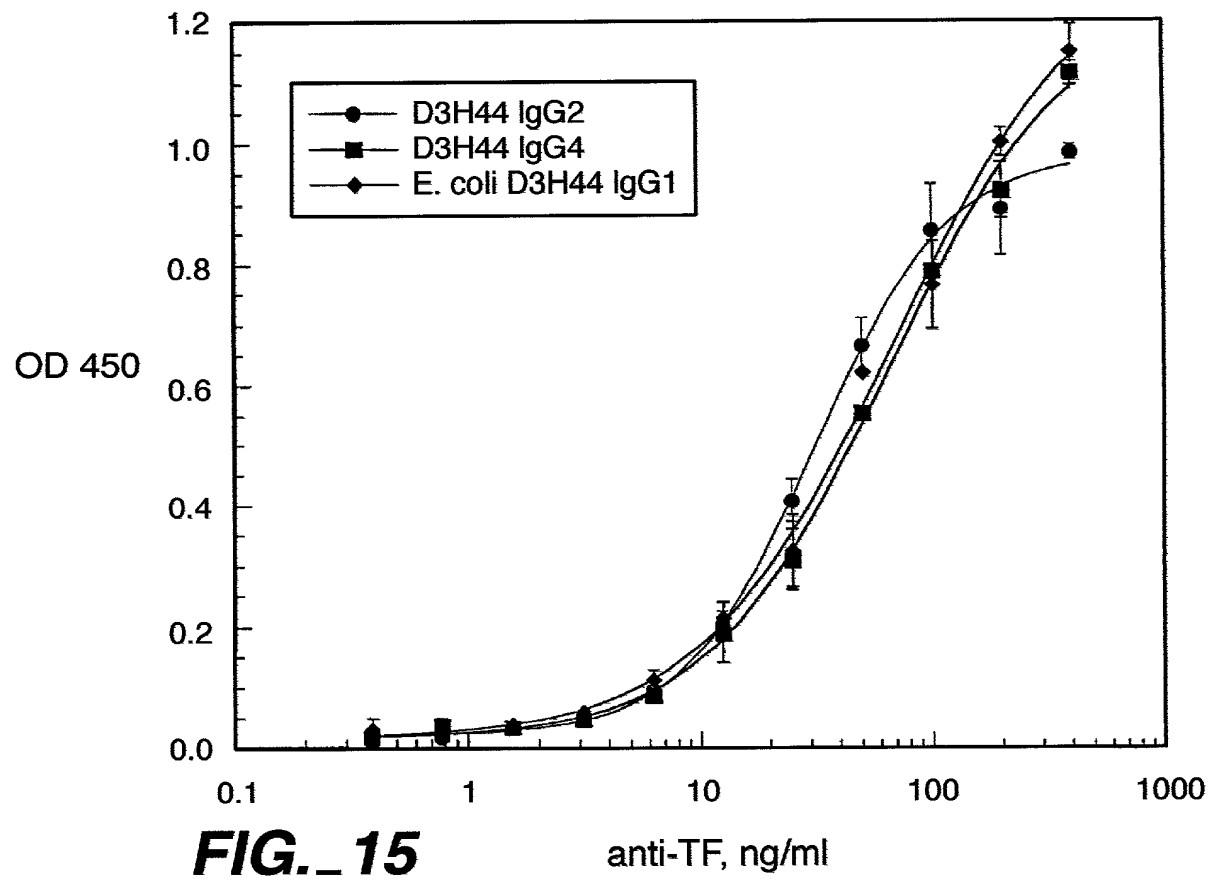
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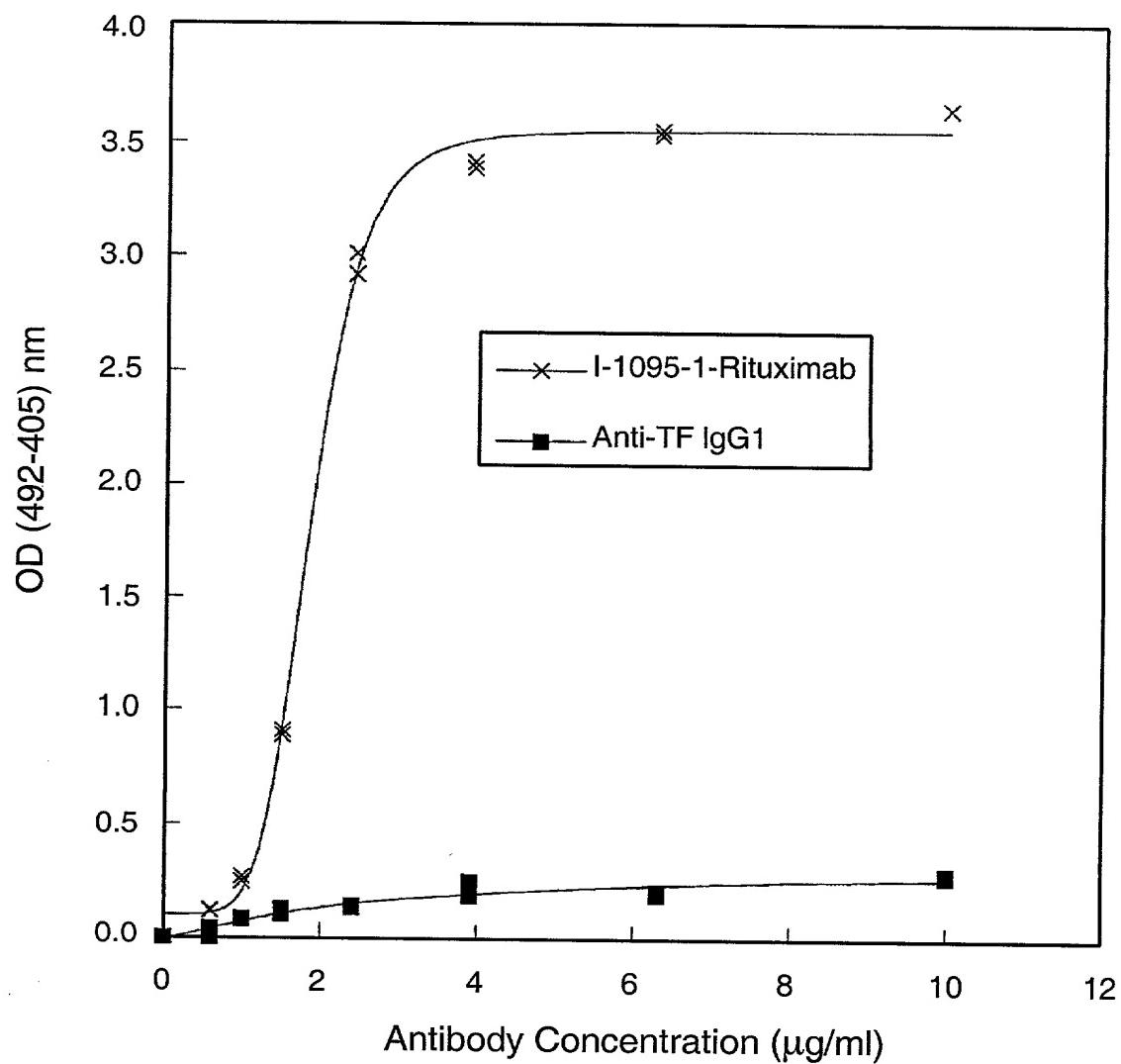
- 1) negative control
- 2) TIR 1-light, TIR 1-heavy, polycistronic
- 3) TIR 3-light, TIR 1-heavy, polycistronic
- 4) TIR 1-light, TIR 3-heavy, polycistronic
- 5) TIR 1-light, TIR 1-heavy, separate cistrons
- 6) TIR 1-light, TIR 3-heavy, separate cistrons
- 7) TIR 3-light, TIR 1-heavy, separate cistrons
- 8) TIR 3-light, TIR 3-heavy, separate cistrons

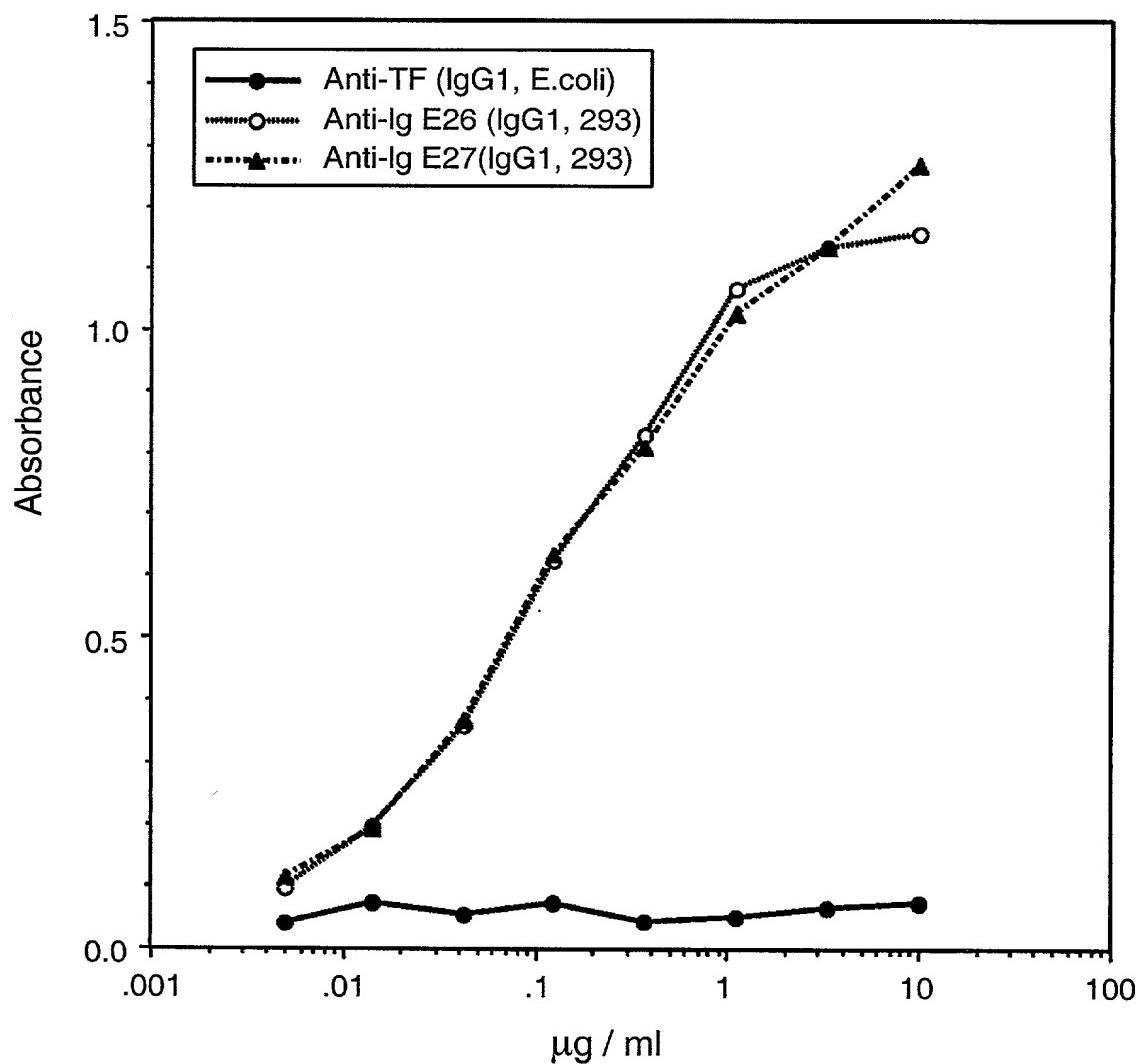
FIG._11**FIG._12**

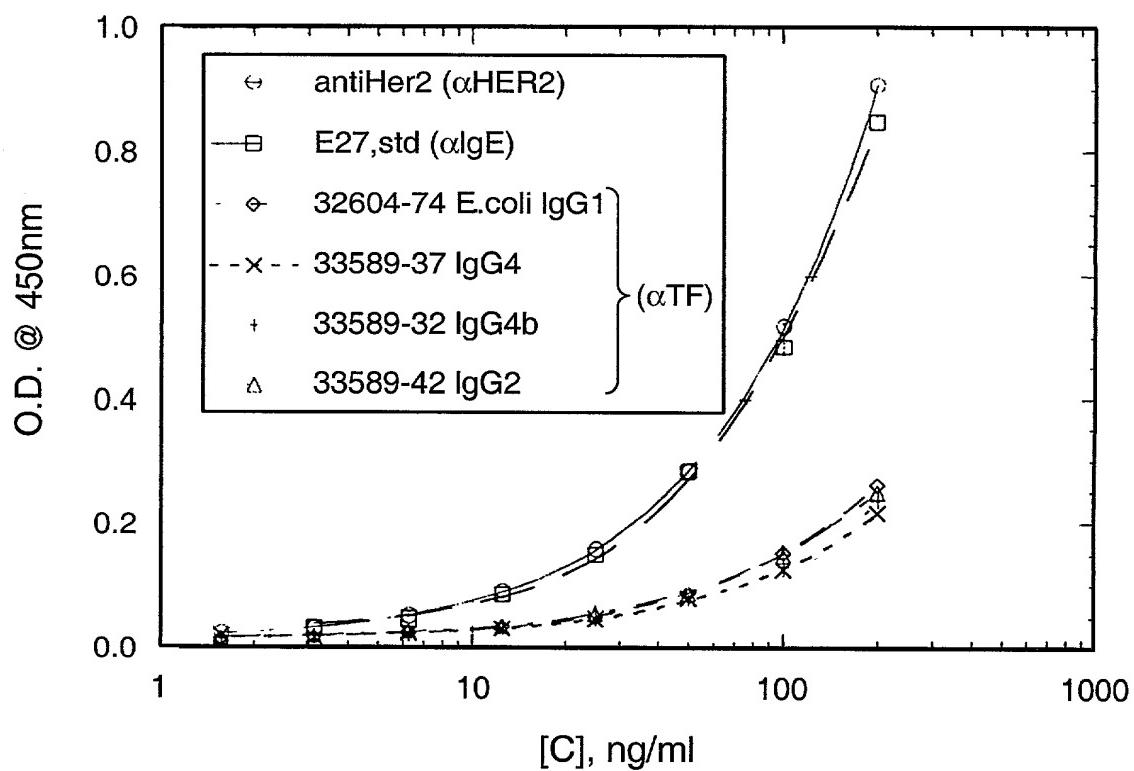
10 / 21

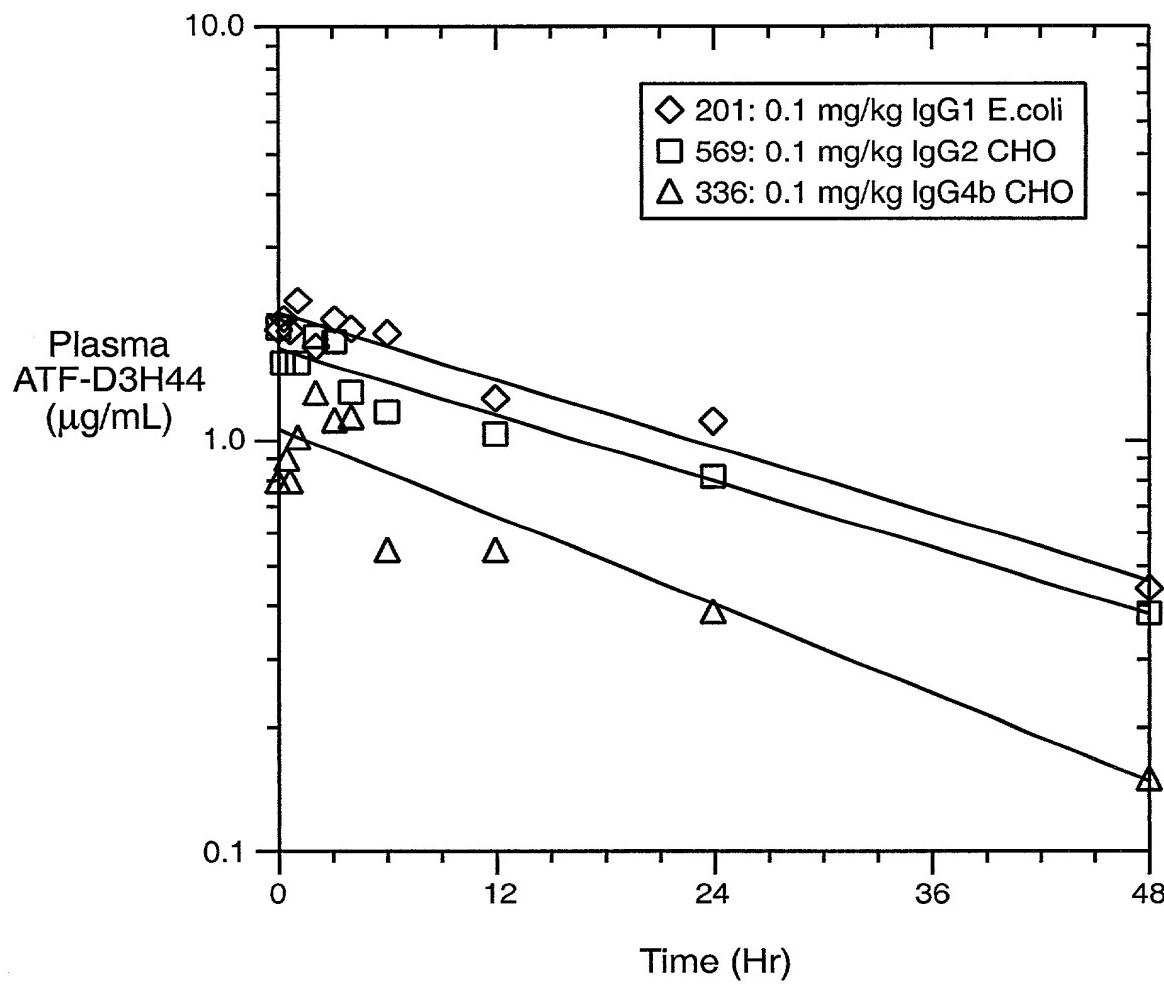
***FIG._13******FIG._14******FIG._15***

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**FIG._16**

**FIG._17**

**FIG._ 18**

**FIG._ 19**

1 GAACTCACT TGGTCACTAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATTTC AACCTTGCCC AAAAAGAAGA AGAGTGAAT
 CTTAAGTGA AGAGGTATGA AACCTATTC TTATGCTG TACTTTAG AGTAACCGT CAACTAAATCAA TCGAACGGG TCTCAGCTTA
 101 GAACTGAGG CGCAGGGAGA AGCTTGGAG ATTATCGICA CTGGCAATGCT TCGCAATATG GCGGAAATG ACCAACAGGG GTTGTATTGT CAGGTAGGG
 CTTGACAC GGTCACT TCGAAACCTC TAATAGCAGT GACGTAAAGA AGCGTATAAC CGCGTTTAC TGGTGTGCG CMACTAACTA GTCCATCTCC
 201 GGGCGTGTGA CGAGTAAAG CCCGATGCCA GCATTCTGA CGACGATAGC GAGCTGCTGC GCCTATTAGT AAAGAAGTTA TTGAAGCATIC CTCGTAGTA
 CCCGCACT GTCCTTTC GGCTACCGT CGTAAGGACT GCTGCTATGC CTCGACGAG CGCTAATGCA TTCTCAAT AACITCGTAG GAGGAGTCAT
 301 AAAAGTAAAT CTTTCAACA GCTGICATAA AGTGTCAAG GCGGAGACT ATAGTGGCTT TGTTTATTT TTTTAAATGTA TTGTTAACTA GTTACGCACT
 TTTCATTA GAAAGCTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA AGCAAAATAA AATATACAT AACATTTGAT CATGGTCA
 401 TCACTAAA AGGGTATCTA GAATTATGAA GAAGAAATTATC GCAATTCTTC TTGCACTAT GTTGTGTTT TCTATGCTA CAAACCGGTAA CGCTGATAJC
 AGTGCATTIT TCCCATAGAT CTTAATACTT CTCTTATAG CGTAAAGAAG AACGTAGATA CZAAGAAAAA AGATAACGT GTTGTGCGAT GCGACTATAG
 M K N I A F L L A S M F V F S I A T N A Y A D I
 1 ^STII Signal Sequence TIR~1 Anti-Tissue Factor Light Chain,
 501 CAGATGACCC AGTCCCCGAG CTCCCTGTC GCCTCTGTC GCGATAGGGT CACCATCACC TCGTGGAGCCA GTGGCGACAT CAAAGAGCTAT CTGAACTGCT
 GTCGACTGGG TCAGGGGTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTGTGG ACGTCTGGT CAGGTGTGTA GACTTGCATA GACTTGCACCA
 26 Q M T Q S P S L S A S V G D R V T I T C R A S R D I K S Y L N W Y 15 / 21
 601 ATCAACAGAA ACCAGAAAAA GCTTCCGAAG TACTGTTTA CTATGCTACT AGTCTGCTG AGGGAGTCCC TCTCTGCTTC TCTGGATCCG GTCTGGCAC
 TAGTGTACT TGGTCCATTG AGGAGCTTC ATGACTTAAT GAACTGATCA TCAAGGAGC TCAAGGAGC TCTCTAGGG AGAACCTAGGC CAAGACCTTG
 60 Q Q K P G K A P K V L I Y Y A T S L A E G V P S R F S G S G S G T
 701 GGATTACACT CTGACCATCA GCAGCTGCA CCATCTGCT TCAATCTGCT GCCATCTGAT GAGTCCTCAT GCACTATGG ACAGGGTAC
 CCTTAATGTA GACTGTAGT CGTCAGACGT CGGTCTCTG AAGCGTGTAA TAATGACAGA AGTCGTGCT CTCGAAACC TGTCCTCATGG
 93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T
 801 AAGGTGCAAGA TCAAAACCAAC TGTTGGCTGCA CCATCTGCT GTCATCTGCTT GCCATCTGAT GAGGTGTTA AACCTGGAAC TGGTCTGTT GTGTGCTG
 TTCCACCTT AGTTGCTTG ACACCGACTT GGTAGACAGA AGTGAAGGG CGGTAGACTA CTCTGTAACT TTAGACCTTG AGCAAGACCA CACACGGACG
 126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
 901 TGAATAACT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTTGGATAAC GCCATCTCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCA
 ACTTATGAA GATAGGCTCT CTCGGTTTC ATGTCACCTT COACCTATTG CGGEGGGTAA GCCCATTGAG GTTCCCTCA CAGTGTCTG TCCTGTGCTT
 160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
 1001 GGACAGGACCC TACAGCTCA GCAAGGAGCT GACGGTGGAGC AAAGGAGACT CGGTGCTAC CAAAGCTAC GCCTGGGAAG TCAACCCATCA GGGCCTGAGC
 CCTGTCGTCGCG ATGTCGGAGT CGTCGTGGGA TGTGCACTCG TTTCGCTGTT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCGGGACTCG
 193 D S T Y S L S S T L T L S K A D Y E K V Y A C E V T H Q G L S
 1101 TCGCCCGTCA CAAGGGCTT CAACAGGGGA GAGTGTAAAT TAAATCCCT ACGCCGAGC CATCGTGGCG AGCTGGTAC CGGGGGATCT AGGCCTAACG
 AGGGGGTAGT GTTCTCGAA GTTCTCCCT CTCACAAATTA ATTAGGAGA TGCGCCATG GGAGCACGC TOCGGATTG
 226 S P V T K S F N R G E C O

FIG._20a

P1793R1

1201 CTCGGTGTGCC GCGGGGGT TTTATTGTT GCGACGGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTGGAGA TTATCGCAC TGCAATGCT
 GAGCCAACGG CGGCCAACAA AAAATAACAA CGGCTGGCA TAGAGCTTAC TTGACACAG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTACGAA

 1301 CGCAATATGG CGCAAAATGA CCAACAGGG TIGATGATC AGGTAGGGG GCGGTGTAC GAGGTAAGGC CCGATGCCAG CAATCTGAC GACCATAACGG
 GCGTTATACC GCGTTTACT GTTGTGTCGCC AACTAATAG TCCATCTCCC CCGGACATG CTCCATTTCG GGTAACGGTC GTAAAGCTG CTGCTATGCC

 1401 AGCTGTGCG CGATTACGTA AGAAAGTTAT TGAAGCTATC AAAGTTAATC TTTCAACAG TTGICATAAA CTGICATAAA GTGICACAGG CCGAGACTA
 TCGACGAGC GCTAATGCAT TCTTCATAA ACTTCATAA AGCTGTAGG AGCACTATT TTCAATTAG AAAAGTGTG CACAGTATT CAACAGTGC GGCTCTGAAAT

 1501 TAGTCGTTT GTTTTATT TTAATGTT TGTAACTAG TAGCTTAAGTT CACGTAAAAA GGTTATCTAG AATTATGAG AAGAATATCG CATTCTCT
 ATCAGGAAA CAAAATAAA AAATTACATA AACATGATC ATGCTTCA GTGCAATTTC CCAATAGTC TTAATACITC TCTTATAGC GTAAAGAAGA
 1 ^STII signal sequence TIR-1

 1601 TCCATCTATG TTGTTTTT CTTCAATTT AAGGAGTACT ACATGCACTG GGTGAGGTTC AGCTGGGTG GCTCTGGGT GGCCTGGGT GGCCTGGGT
 ACCTAGATAC AAGCAAAAA GATAACGATG TTGCGCATG CGACTCCAAG TCGACCCACCT TCCGGACCT TACCCAACTT AACTAACTAG
 10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
 ^Anti-Tissue Factor Heavy Chain

 1701 TGTCTGTG CAGCTCTGG CTTCAATTT AAGGAGTACT ACATGCACTG GGTGAGGTG CCGGGCCAT TCCGGACCT TACCCAACTT AACTAACTAG
 ACAGGACAC GTGGAAGAC GAACTTAA TCCCTCATGA TGTACGTGAC CGACTGAGTC CGAGGAGTC CGGGGCCAT TCCGGACCT TACCCAACTT
 43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

 1801 CAGGAAAGG CAACAGGATC TATGACCCGA AGTTCAGGA CGTGTGCACT ATAAGGCGCTG ACAATTCCAA AAACACAGCA TACCTGGAGA TGAACAGGCT
 GTCTGTCTC GTTGTGCTAG ATATGCTCTC TCAAGGCTCT GGCACGGTGA TATTCGAC TGTAAAGTT TTGTTGCTGT ATGGACGCT ACTGTGCGGA
 77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S 1

 1901 CGGTGTGAG GACACTGCGC TCTTATTG TGCTCTGAGAC ACGGACCTCTG TGCAGCTGAGAC AGTTCAGTA CTTGGGTCA GAAACCTGG TCACCGTCTC
 CGCACGACTC CTGTACGCC AGATAATAC ACGGACCTCTG TGCAGCTGAGAC AGTTCAGTA CTTGGGTCA GAAACCTGG TCACCGTCTC
 110 R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V T V S S A S

 2001 ACCAAGGGCC CATCGTCTT CCCCTGCCA CCCTCTCCA AGGACACCTC TGCGGACA CGGGGCTGG CCTGGCTGGT CAAGGACTAC TTCCCCGAAAC
 143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P
 ^STII signal sequence TIR-1

 2101 CGGTGACGGT GTCTGGAAAC TCAAGGGCCC TGACCAAGACCC CGTGCACACC TTCCGGCTG TCTTACAGTC CTCAAGTC TACTCCCTCA GCACCGTGGT
 GCGCACTGCCA CAGGACCTCTG AGTTCGCGGG ACTGGTGCCTC GCACGTGGG AGGAGTGTAG GAGTCGTAG ATGAGGGAAT CGTGGCACCA
 177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V

 2201 GACTGTGCC TCTAGGAGCT TGGGACCCA GACCTACATC TGCAACGTA ATCACAGGCC CAGGAAAGCC AAGGGCGAC AGGAGTGTAG TCTTCAACT CGGGTTAGA
 CTGACACGGG AGATGTGCGA ACCCGTCTGG TTCCACCTGT GTCTGGTTAG ACGTGTGACT TCTTCAACT CGGGTTAGA
 210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S

FIGURE 20b

2301 TGTGACAAA CTCAACACATC CCGACCGTCG AACCTCTGGG GGGACCGTCA GCTCTCTCT TCCCCCAA ACCCAAGGC ACCCTCATGA
 243 ACATGTTT GAGTGTGTAC GGTGGCACG TTGGTGGAC CCCTGGAGT CAGAAGGACA AGGGGGTTT TGGGTTCCTG TGGZAGTACT
 2401 TCTCCGGAC CCCTGGAGTC ACATGGTGCG ACCACCTGCA CTGGGTGCTT AGTTCAGTT GACCATGGAC CTGGCCGACCT TCCACGATT
 AGAGGGCTCG GGEACTCCAG TGTACGGAC ACCACCTGCA CTGGGTGCTT S H E D P E V K F N W Y V D G V E V H N
 277 S R T P E V T C V V D V S H E D P E V K F N W Y V D G V E V H N
 2501 TGCCAAGACA AAGCCGGGG ACCAGGAGTA CAACAGGACG TACCGGTGG TCAGGGTCTT CACCGGACT GGTGTAATGG CAAGGAGTAC
 ACCCTTCTT TTCCGGCCC TCCCTGTCAT GTTGTGTCAT AGTGGCACAC AGTGGAGGA GTGGCAGAAC CGCACTTACCGTTCCTG
 310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y
 2601 AAGTGGAGG TCTCCAAACAA AGCCCTCCAA GCCCCATCG AAAGAAACAT CTCCAAGGCC AAAGGGCAAGC CCCGAGAACCC
 TTACGTTTC AGAGGTTGGT TCGGGAGGT CGGGGGTAGC TCTTGGTA GAGGTTCGG TTTCCTGG GGGCTCTGG TGTCCACAT TGGAACGGGG
 343 K C K V S N K A L P A P I E K T T S K A K G Q P R E P V Y T L P P
 2701 CATCCGGGA AGAGATGACC ACAACCGG TCAAGCTGAC CTGGCTGAC AAAGGTTCT ATCCCAGCGA CATCGCCGTG GAGTGGGAGA GCAATGGCA
 GTAGGGCCCT TCTCTACTGG TTCTGGTC AGTGGACTG GACGGACCG TTTCGGAGA TAGGGTGGCT GTAGGGCAC CTACCCCTCT CGTACCCGT
 377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q
 2801 GCGGAGAAC AACTACAAGA CCACGGCTTC CGTGGCTGGAC TCGGACGGCT CCTTCTCTCTT CTACAGGAAG AGCCTCTCC
 CGGGCTCTTG TTGATGTTCT GGTGGAGGG GCACGACCTG CGACTAGTA CTGGAGAGC TGTGGTGTAC GATGTCGTC
 410 P E N N Y K T T P V L D S D G S F L Y S K L T V D K S R W Q Q / 17
 2901 GGAAAGCTCT TCTCTAGTCG CGTGTAGCAT GAGGGCTCTGC ACAACCACTA CACGGAGAG AGCCTCTCC
 CCCTTGAGA AGAGTAGAG GCGTTTTTA TGTGTAACTC ATGTTGACA GCTTATCAGC GATAAGCTT ATGGGGTAG TTATAAGCA
 443 G N V F S C S V M H E A L H N Y T Q K S L S P G K O / 21
 3001 CTAGAGTCCC TAACGCTGGG TGGGGCTGGG GCGTTTTTA TGTGTAACTC ATGTTGACA GCTTATCAGC GATAAGCTT ATGGGGTAG
 GATCTCAGGG ATTGGAGGC AACGGGGCC CGCAAAAT ACAATTGAG TACAATCTGT CGAATAGTAG CTATTGAAA TTACGCCATC
 3101 TAAATTGCT AACATGGCT AACATGGCTT ATGAAATCTA GGCACCGTGT ATGAAATCTA AACATGGCTT CTCGGCTACG
 AATTTAACCA TTGGCTAGT CGTGGCACA TACTTATGAT TTGTTACGCA GTAGGAGTAG AGTGGACCT ACCACATCG TATCGAAC
 3201 TTATGGGGT ACTGGGGGC CTCTGGGGG ATATGTCCTA TICCTGGGGG ACTATGGGT GCTGCTAGGC CTATATGGT TGATGCAATT
 ATATAGGGCCA TGACGGCCG GAGAACGCC TATAGGAGGT AAGGCTCTG TAGGGCTAG TGATACGCA ACTACGTTAA

"Start Tet Resistance Coding Sequence

1 GAATTCAACT TCTCCATACT TGGATAAGG AAATACAGAC ATGAAATAC TCATTGCTGA GTTGTATT AAGCTGCC AAAAGAAGA AGAGTCGAA
 CTTAAGTGA AGAGGTATGA AACCTATTCC TTATGCTG TACTTTTG AGTAAGCCT CAACAATAAA TTGCAACGGG TTTTCTCTCT TCTCAGCTTA
 101 GAACTGTG CGCAGGTAGA AGCTTGGAG ATTATGTCA CGGCAATGCT TCGCAATATG GCGCAAATG ACCAACAGGG GTTGATTGAT CAGTAGGG
 CTTGACAC CGGTCATCT TCGACAC GCGTTCATCT TAATAGCAGT GACGTAGA AGCGTATATAC CGCGTTTAC TGTTGTCGC CAACTAACTA GTCCATCTCC
 201 GGGGCTGTA CGAGGTAAG CCCGATGCCA GCATTCTGA CGAGGATACG GAGCTGTGC CGGATTACG TAAAGAAGTAA TGAAGCTTA TTCTCTCAAT AACTCGTGA
 CCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT CGTGTATGC CTGCAAGAC CGCTAATGCA TTGTTTAACT AACTCGTGA GAGCAGTCAT
 301 AAAAGTTAACTTTCACCA GCTGTATMA AGTGTCAAG GCGGAGACTT ATAGTCGCTT TGTGTTTAACT TTTATGTA TTGTAACTA GTACCGAAGT
 TTTCAATTAA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGA TATCAGCGAA ACAAAATAAA AAAATTACAT AACATTGAT CATGGTCA
 401 TCACGTAAGA AGGGTATCTA GAATTATGAA GAATTATGAA TGTGCTCTAT GTGCAATCTAT GTTCGTTT TCTATGCTA CAAACGGTA CGCTGATATC
 AGTGCATTTCCTTAATCTTCAAGTAACTT CTCATAGAT CGTAAAGTAG AACGTAGATA CAAAGAAAA AGATAACGAT GTTGGCCAT GCGACTATAG
 1 M K K N I A F L L A S M F V F S I A T N A Y A D I
 *STII signal TIR ~1
 *Anti-VEGF Light chain^

501 CAGTGCACC AGTCCCAGG CTCCCTGTC GCCTCTGGT GCGATAGGGT CACCATCAC CTCAGGCACAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
 GTCAACTGGG TCAAGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGGGT ACGTGTGGT CAGTCCTATA ATCGTCGTTAA AATTCGACCA
 26 Q L T Q S P S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y 18 / 21
 601 ATCAACAGAA ACCAGAAAA GCTCCGAAAG TACTGATTAA CTTCACCTCC TTCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGAC
 TAGTGTCTT TGGTCTCTT CGAGGCTTC ATGACTAAAT GAAGTGGAGG AGAGGGTGA GACCTCAGGG AAGAGGAAG AGACCTAGGC CAAGACCTTG
 60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T
 701 GGATTCACT CTGACCATCA GCACTGCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTTCCGT GGACGTTGG ACAGGGTAC
 CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTCTG AAGGGTGA TAATGACAGT TGTCAATCG TGGCACGGCA CCTGCAAAACC TGTCCTATGG
 93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
 801 AGGGGAGA TCAAAGAAC TGTGGCTGCA CCATCTGCT TCACTCTGAT GAGGAGTGA AATCTGAAAC TGCTCTGTGTT GTGTCCCTGC
 TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAAAGGG CGGTAGACTA CTCGTCAACT TTGACCTTG AGCAAGACAA CACACGGAC
 126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
 901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GTGGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGGT GTCACAGAGC AGGACAGCAA
 ACTTATTGAA GATAGGGCTC CTCCGGTTTC ATGTACCTT CCACCTATTG CGGGAGTTA GCCCATTGAG GTGTCTCA CAGTGTCTCG TCCTGTGTT
 160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
 1001 GAGACGAC TACGCTCA CGAGCACCT GACGCTGAGC AAAGCAGACT AGGAAACA CAAAGTCTAC GGCCTGGAAAG TCACCCATCA GGGCCTGAGC
 CCTGTCGTGG ATGTGGAGT CGTCGTGGGA CTGGGACTCG TTGCTCTGTA TGCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
 193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
 1101 TCGCCCGTCA CAAAGAGCTT CAAACAGGGAA GAGTGTAAAT TAAATCCTCT AGCTGGCG AGCTGGTAC CGGGGATCT AGGCCTAACG
 AGGGGGCAGT GTTCTCGAA GTTGTCCCCCT CTCACAAATT ATTAGGAA TCGGACCGC TCGACCCATG GCGCCCTAGA TCCGGATTGC
 226 S P V T K S F N R G E C O

FIG._21a

1201 CTCGGTTGCC GCCGGCCCTT TTTATTGTT GCCGAGCGGC ATCTGGATG AACTGTGTC GCAAGTAGAA GCTTGGAGA TATGGTAC TGCAATGCTT
 GAGCCAACGG CGGCCCGCAA AAAATACAA CGGCTGGCG TAGAGCTAAC TTGACACAGC GTTCCATCTT CGAACCTCTT ATAGGAGTG ACGTAGAA
 1301 CGCAATATGG CGCAAAATGA CCAACAGGGG TTGATGATC AGGTAGAGGG GGGGTGTAC GAGTAAGG CCGATGCCAG ATTCCCTGAC GACGATAACGG
 GCGTTATACC GCGTTTACT GTTGTGCGC AACTAATAG TCCATCTCCC CGGACATG CTCCATTTCG GGCTAAGGTG GTAAGGACTG CTGCTATGCC
 1401 AGCTGCTGG CGATTACGTA AGAAAGTTATGAGTCAAACTTCAAA TGTCAATTAG AAAAGTTAG TTTCATTAG AAAGTGTCAAGTCTGAACTT
 TCGACGACCC GCTAATGCTT TTCTTCATAA ACTTCGAGG AGCACTTACGTTTCAATTAG AAAAGTTAG GACAGTATT CAACAGTCCC GGCTCTGAAAT
 1501 TAGTCGCTT GTTTTATT TTAATGTT TTGTAACCTAG TAGCAAACTT CACGTAAGT AATTTGAAAG AAGATATCTAG CATTCTCT
 ATCAGGAAA CAAAATAAA AAATTACATA AACATGATC ATGCGTCAA GTGCATTTC CCCATAGATC TAAATACATTC TTCTTATAGC GTAAAGAAGA
 1

1601 TGGCATCTATG TTGCTTCTTCTT CTATGGTAC AAACGGTAC GCTGAGGTT AGCTGGTGA GTCTGGGGT GGCTCTGGTGC AGGCCGGGG CTCACTCCGT
 ACGTAGATAC AAGCAAAAAA GATAACGATG TTGGCATG CGACTCCAG TCGACCACTT CAGACCGCCA CGGACCAAG TGCGTACCCCC GAGTGAGGCA
 10 A S M F V F S I A T N A Y A E V Q L V E S G G G L V Q P G G S L R

^Anti-VEGF Heavy Chain

1701 TTGTCCTGTG CAGCTCTGG CTAGCACTTC ACGCACTACG GTATGAACGT GGTCCGTCAG GCCCCGGGTA AGGGCTGGGA ATGGCTGGGA TGGATTAACA
 AACAGGACAC GTCGAAGACC GATGCTGAAG TGCCTGATGC CATACTGAC CCAGGAGTC CCGGGCCAT TACCCAACTT ACCTAACTT ACCTAACTT
 43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T

1801 CCTATAACGG TGAACCGACC TATGCTGGGG ATTCAAAACG TCGTTCTACT TTTCCTTTAG ACACCTCCAA AAGCACAGCA TACCTGGAGA TGAACAGCCT
 GGATATGGCC ACTTGCTGG ATAGGACGCC TAAAGTTGC AGCAAAAGTCA AAAAGAACATC TGTGGAGGT TTCTGTCGT ATGGACGTCT ACTTGCTGGAA
 77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

1901 GCGCGCTGAG GACACTGCG TCTATTACTG TGCAAACTAC CGTACTATT ACGGCACGAG CCACTGGTAT TTGAGCTGTCT GGGGTCAAGG AACCCCTGGTC
 CGCGCGACTC CTGTGACGGC AGATAATGAC ACGTTCTATG GGCATGATAA TGCGGGCTC GTGAGCCTAA AAGCTGGAGA CCCCACTTCC TTGGGACCAAG
 110 R A E D T A V Y Y C A K Y P Y Y G T S H W Y F D V W G Q G T L V

2001 ACCGCTCTCC CGGGCTCCAC CAAGGGCCCA TCGGTCTTCC CCGGTGCACCTC CTCCTCCAAG AGCACCTCTG GGGCACAGC GGCCCTGGGC TGCTCTGGTC
 TGGCAGGAGA GCGGGAGGT GTTCCGGGT AGCCAGAAGG GGGACCGTGG GAGGAGGTTC TCGTGGAGAC CCCGGTGTG CCGGACCCG ACGGACCAAGT
 143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

2101 AGGACTACTT CCGGGAAACCG GTGACGGTGT CGTGGAACTC AGGGGCCCTG ACCAGGGGG TGCCACACCTT CCCGGTGTGCT CTAAGCTCTT CAGGACTCTA
 TCCGTATGAA GGGCTGGC CACTGCCACA GCACCTTGAG TCCGGGGAC ACGTTGGAA GGGCCGACAG GATGTCAGGA GTCTGAGAT
 177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCCTCAGC AGGTTGGTGA CTGTGCCCTC TAGGAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAAGGCCCA GCAACACCAA GTGGACAAAG
 GAGGGAGTGC TCGGACCACT GACACGGGAG ATCGTGAAC CGGTGGGTCT GGATGTAGAC GTTGACTTA GTGACTTA GTGACTTA GTGACTTA GTGACTTA
 210 S L S V V T V P S S L G T Q T Y I C N V N H K P S N T K V D K

^STII Signal TIR~1

FIG.-21b

2301 AAAGTTGAGC CCAAAATCTTG TGACAAACT CACACATGCC CACCGTCCC AGCACCTGAA CTCCTGGGG GACCGTAGT CTTCCTCTC CCCCAAAC
 TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGTACGG GTGGCACGGG TCGTGTGACTT GAGGACCCCT CGGGAGCTCA GAAGGAGAAG GGGGCTTTG
 243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
 2401 CCAAGGACMC CCTCATGATC TCCCCGACCC CTGAGGTAC ATGGGTGGTGC ATGGAGTCAGA GCGCACGAAGA CCCTGAGGTC AAGTTCAACT GGTACGTGGA
 GTTCTCTGTG GGAGTACTAG AGGGCCTGGG GACTCAGTG TAGCCACAC CACCTGCACT CGGTGCTCT GGGACTCCAG TCAAGTGA CCATGACCT
 277 K D T L M I S R T P E V T C V V D V S H E D P E V K F N W Y V D
 2501 CGGGGTGGAG GTGGCATTAATG CCAAGACAAA GCGCGGGAG GAGGAGTACA ACAGCACGTA CGGTGCTCA AGCGTCTCTCA CGGTGCTGCA CCAGGACTGG
 GCGGCACCTC CACGTATTAC GTTCTGTGTT CGGGGCTTC CTGGACCCCT TCGTGTGCACT TGTGTGAT GGCACACZAG TCGGAGGAGT GGCAGGACGT GGTCTGTGACC
 310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
 2601 CTGAATGGCA AGGAGTACAA GTGCAAGGTC TCCAACAAAG CCCTCCCGAG CCCATCGAG AAAACCATCT CCAAGCCAA AGGGCAGCCC CGAGAACAC
 GACTTACCGT TCCTCATGTT CACGTTCCAG AGGTGTTTC GGGTAGCTC TTTGGTAGA GTTTCGGTT TCCCGTGTGG GCTCTGGT
 343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
 2701 AGGTGTACAC CCTGCCCA TCCCAGGAG AGATGACCAA GAACCAAGGTC AGCCTGACCT GCCTGGTCA AGGCTCTAT CCCAGGACA TCGCCGTGGA
 TCCACATGTT GGACGGGGT AGGGCCCTTC TCTACTGGT CTGGTCCAG TCGGACTGGA CGGACCACTT TCCGAAGATA GGGTGGTGT AGGGACACCT
 377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
 2801 GTGGGAGAGC AATGGCAGC CGGAGAACAA CTACAAGACC AGCGCTCCCG TGCTGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACCGTGGAC
 CACCCCTCTG TTACCGTCTG CCCTCTGGT GATGTTCTGG TGCGGGAGGGC ACGACTGAG GTGCGCGAGG AAGAAGGAGA TGTGTTGCA GTGGACCTG
 410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
 2901 AAGAGGAGGT GGCAGGAGG GAAAGTCTTC TCATGCTCCG TGATGCTGA GGCTCTGCAC ACCACTACA CGCAGGAGAG CTCCTCCCTG TCTCCGGTA
 TTCTCGTCCA CGGTGCTCC CTGGAGAAG AGTACGAGGC ACTACGTACT CGGAGACGTG TTGGTGTATGT GCGTCTCTC GGAGGGAC AGAGGCCCAT
 443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
 3001 ATAAGGATG CGACGGCCCT AGAGTCCCTA AGGCTGGTT GCGGCCGGC GTTTTATT GTAATCTCAT GTTGTACAGC TTATCATCGA TAAGCTTAA
 TATTGCTAC GCTGCCGGAA TCTCAGGGAT TGGAGCCAA CGCGGCCCG CAAAAATAA CAATGAGTA CAAACTGTCG ATATACTGCT ATTGAAATT
 477 O
 3101 TGGGGTAGTT TATCACAGTT AAATTGCTAA CGCAGGTCAGG CACCGTGTAT GAAATCTAAC ATGCGCTCA TCGTCTATCCT CGGCACCGTC ACCCTGGATG
 AGGCCATCAA ATAGTGTCAA TTAACGATT GGGTCACTA CTTAGATTG TTACGCGAGT AGCAGTAACTA CTTAGATTG TTACGCGAGT AGCAGTAACTA
 ^Start Tet Resistance Coding Sequence

3201 CTGTAGGCAT AGGCTGGTT ATGCCGGTAC TGCCGGCT TATGGCTCAC TATGGCTCAC CGGACAGCAT CGGTGCTGCTG TGCTAGGCT
 GACATCCGTA TCCGACCAA TAGGCCATG ACGGCCATG ATACGCCATG TAGGAGTAA GGCTGTGCTA GCGTGTGCTA ACGATCGGCA
 3301

FIG.-21c

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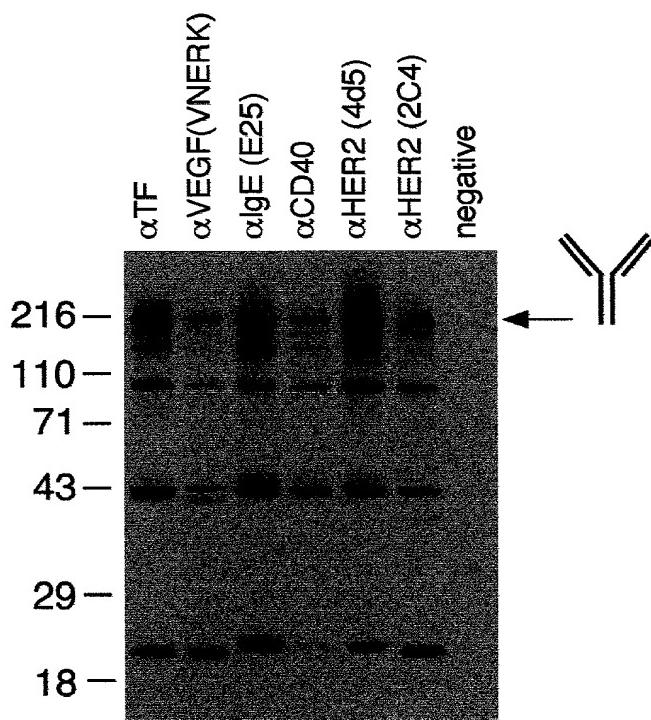


FIG._22A



FIG._22B